these cases little food can be absorbed, such sources of energy as are available must be conserved by keeping the patient thoroughly warm—in bed for preference—and by limiting exercise as far as possible.

The ultimate fate of the majority of "coeliac" cases is recovery, but even after what may be regarded as complete recovery there is always a tendency to recidivism, and some dilatation of the intestines usually persists.

Type 3.

As I have already indicated, the symptoms of certain forms of dyspepsia are so remote and general that they are liable to be attributed to tuberculosis or other constitutional trouble, rather than to actual defects in the digestive processes. The kind of case which I am about to describe is essentially of this character in its most typical form. It occurs in children between 2 and 16 years of age. It is chronic and remittent in character.

Children suffering from this form of dyspepsia are never really well, neither do they look well. They usually do not complain of feeling ill, but they have little energy, are easily tired, and have capricious appetites. There is often a continued temperature, usually under 100° F., sometimes lasting for many months. The complexion is sallow, with dark rims to the eyes, the tongue is dirty, and the breath tainted. There is irritability of temper, restlessness at night, or night terrors. The children often complain of abdominal pain or stitch in the side on running. The urine is usually thick, cloudy, or ammoniacal, and the stools are offensive. One of the most diagnostic and characteristic of the symptoms is the regular manner in which periodic attacks of biliousness supervene. These symptoms make up a clinical picture which must be perfectly familiar to everyone; but since all of them in combination never occur in one case the presence of even a few of them should put the practitioner on his guard.

All these symptoms can be rationally and satisfactorily explained on the assumption that the food consumed is not completely digested, owing either to its quality or total quantity, or to the relatively deficient powers of the digestive functions to cope with the task imposed upon them. Whatever may be the cause bringing about this failure of digestion the result is the same. Food which should have been digested normally by the normal enzymes of the alimentary tract remains undigested, or only partially digested, and becomes the pabulum of bacteria in the large bowel, and, as a consequence, the colon assumes an unhealthy condition, with offensive stools, flatulence, abdominal pains, and stitch in the side. This stitch in the side, so very characteristic of intestinal toxæmia, is, I believe, caused by the dragging of a heavy and sagging colon on its two points of support—its hepatic and splenic flexures—a dragging which is intensified by exercise in the upright position.

The toxic products of intestinal putrefaction are absorbed and carried to the liver, where for a time they may be effectually dealt with and rendered innocuous. Failure, however, is evidenced by offensive breath, dirty tongue, irritability, and other nervous symptoms. After varying periods of endurance the liver breaks down in function, and then the systemic circulation is inundated with a flood of unaltered toxic products, with intensification of the nervous symptoms, which take the form of vomiting, high temperature, migraine, or sick headache.

Under these conditions, and especially owing to the vomiting, the further consumption of food becomes impossible, and the liver obtains a much-needed rest. General recovery then takes place, the appetite returns, and the whole cycle of events is repeated with systematic regularity. The treatment of these bilious attacks, or cyclic crises, is usually by calomel or grey powder. This treatment, which as a rule gives immediately good results, is not really rational or far-seeing, for its efficacy is mainly due to stimulation of the liver, and not to removal of the cause. It acts, in fact, on the principle of "spurring on the tired horse," instead of taking the load off its back. The toxic bodies which directly bring about these breakdowns of liver function are due to the decomposition of nitrogenous foods, such as butcher's meat, fish, eggs, poultry, and milk. Hence it is obvious that the treatment should be concerned with a limitation of the intake of these particular

foods. On the other hand, the fermentations which take place in carbohydrate and cereal foods lead to the formation of considerable quantities of acid bodies, such as acetic acid, butyric acid, lactic acid, propionic acid, and so on; these do not seriously tax hepatic function after absorption, but they do seriously drain the bicarbonate reserves of the blood and lead to those true conditions of acidosis which so often complicate the actual hepatic crisis. It should be clearly recognized that conditions of acidosis proper, in which there is a reduction of the alkaline reserves of the blood, should be distinguished from conditions of ketosis in which there is usually acetone in the blood, the breath, and the urine. A true ketosis seems to be one of the results of defective fat metabolism and hepatic insufficiency, and therefore it is scarcely to be wondered at that in these cases of periodic liver attacks due to intestinal toxæmia the condition should be complicated by a ketosis. In fact, I think it may be assumed with some confidence that in cases of intestinal toxæmia due to defective digestive processes there is generally a combination of all these conditions—hepatic crisis, ketosis, and true acidosis. The rational treatment of these cases involves three main principles of therapeutics: First, and mainly, the limitation of nitrogenous foods. Secondly, the limitation of all foods within the bounds of physiological requirements. Thirdly, the prevention as far as possible of intestinal decomposition by sterilization of the intestinal tract. Finally, by the prevention of conditions of true acidosis by the free administration of alkalines.

I hope that the three types which I have chosen to illustrate my thesis will help to show that if the digestive functions are imperfectly performed certain immediate, and, if I may use the term, proximal, symptoms, are liable to be produced which are mainly concerned with disturbances of the neuromuscular mechanisms that control the transit of food through the alimentary tract. These symptoms carry a warning note which, if attended to, should obviate the development of other, more serious and more distal, symptoms connected with the breakdown of liver function and with the poisoning of the system with various toxic substances.

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THE SIGNIFICANCE OF INTRADERMAL TUBERCULIN TESTS.

A PRELIMINARY NOTE ON AN INVESTIGATION IN PROGRESS BY
THE MEDICAL STAFF OF THE WELSH NATIONAL MEMORIAL
ASSOCIATION.

BY

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THE intradermal method of tuberculin testing was introduced by Mendel¹ and Mantoux² in 1908. For quantitative tests it has the advantage over the von Pirquet reaction in that the whole of the tuberculin used does actually enter the tissues. Happ and Casparis³ consider that 0.01 mg. of tuberculin given intradermally corresponds to the usual von Pirquet test. While the von Pirquet test carried out according to the technique described by me in the *British Medical Journal* of February 2nd, 1924, appears to give results equivalent at least to 0.1 mg. of tuberculin intradermally, there can be no question but that the intradermal method is a much more sensitive test than the cutaneous one, and gives a greater amplitude in the elicitation of latent infection.

As compared with the subcutaneous tuberculin test, the intradermal method aims at a local, not a general, reaction, and it is an interesting fact that doses of tuberculin capable of giving rise to severe focal and constitutional reactions in infected persons can be given intradermally without exciting any appreciable response other than the local one at the site of inoculation. An excellent account of this and other forms of the tuberculin test was given by Burhans⁴ in 1927, and should be consulted by all interested in the subject.

At a meeting of the medical staff of the Welsh National Memorial Association in December, 1927, it was decided to test out the intradermal method on various types of tuberculous patients with a view to arriving at a clearer idea of its significance in relation to the disease. As director of research to the association it has fallen to my lot to draw up a scheme of investigation, co-ordinate the work, and analyse the results; but nearly all the actual tests have been carried out by my colleagues of the medical staff of the association, and in particular by Drs. D. W. Fenwick Jones, D. H. Mills, and L. R. Clark; and for all this help I desire to express my gratitude. I also wish to thank Dr. R. A. O'Brien, director of the Wellcome Physiological Research Laboratories, through whose kindness a very reliable sample of old tuberculin (O.T. No. 1154, B. W. and Co.) was made available for use in all the tests now recorded. This tuberculin was put up by me in the following strengths, and supplied, as required, to the medical staff: 1 in 10,000, 1 in 5,000, 1 in 1,000, and 1 in 500. The diluent used was sterile normal salt solution to which 0.5 per cent. of carbolic acid was added. Medical officers were warned that diluted tuberculin is liable to deteriorate, and that the phials should be regarded as unreliable three weeks after the date of issue. The inoculations were given intradermally, a volume of approximately 0.1 c.cm. of the appropriate dilution being injected by means of a whole-glass hypodermic syringe with a very fine accurately fitting needle. It was found that needle No. 214, B. W. and Co., was suitable for the purpose. Special precautions were taken to avoid too deep a puncture. The escape of tuberculin into the subcutaneous areolar tissue vitiates the test and exposes the patient to the risk of a general reaction. The site chosen was usually the outer surface of the arm a few inches below or above the elbow-joint. No injection was considered satisfactory if it did not raise a circumscribed wheal at the point of inoculation. It was decided not to give "control" injections of sterile diluting fluid, though these are advocated by Burhans.

The number of inoculations to which patients will submit is limited, and it is my experience that "reactions" after such control inoculations are so very rare as to be practically negligible. In the majority of cases a positive reaction with any given "dilution" was accepted as a proof that the patient concerned would be positive with the stronger preparations—that is, a patient reacting to 1 in 10,000 was assumed to be positive also to 1 in 5,000, 1 in 1,000, and 1 in 500. That this assumption, which underlies the percentages in the following records, is correct, was proved by the results in those few patients to whom all four strengths were given. In these it was found that the intensity of the reaction increased regularly with each increase in strength of tuberculin.

Comparison of Reaction in Healthy Adults and Tuberculous Patients.

A group of 46 healthy male adults residing in London was tested by me according to the technique above described except that only two dilutions of tuberculin—1 in 5,000 and 1 in 1,000—could be used. To these healthy volunteers, who desire to remain nameless, my sincere thanks are due. The results in this healthy group were compared with the results in 150 tuberculous patients, a miscellaneous group including adults and children, males and females, pulmonary and non-pulmonary, under treatment by the association. The findings are compared in Table I.

TABLE I.—*Tuberculin Reactions in the Healthy and the Tuberculous.*

Tuberculin Dilutions.	Percentages Positive.		Average Size of Reaction in Centimetres.*	
	Healthy.	Tuberculous.	Healthy.	Tuberculous.
1 in 10,000		37		0.5
1 in 5,000	80	61	1.30	1.0
1 in 1,000	93	70	2.07	1.4
1 in 500		74		1.6

* All the reactions in the "healthy" group, but only 37 reactions in the tuberculous group, were measured.

It will be apparent from the above table that, both in the percentages of positives and in the extent of the raised area of reaction, the healthy persons gave results over 20 per cent. higher than the persons actually suffering from tuberculosis. This finding raised the question of the relation, if any, of tuberculin sensitivity to the severity of the disease; and the above miscellaneous group of patients was now analysed according to clinical type.

Comparison of Pulmonary and Non-pulmonary Cases.

Pulmonary tuberculosis is, on the whole, more severe than non-pulmonary tuberculosis; so a comparison was made between 64 pulmonary and 83 non-pulmonary patients, the latter constituted, for the most part, of cases of bone and joint tuberculosis.

TABLE II.—*Tuberculin Reactions in Pulmonary and Non-pulmonary Cases.*

Tuberculin Dilutions.	Percentages Positive.		Average Size of Reaction in Centimetres.*	
	Pulmonary.	Non-pulmonary.	Pulmonary	Non-pulmonary.
1 in 10,000	26	45	0.50	0.40
1 in 5,000	54	70	0.80	1.38
1 in 1,000	66	77	1.30	1.24
1 in 500	72	78	1.58	1.60

* Only about 15 patients in each group were "measured" in all dilutions.

Here again the less severe and non-pulmonary group gives higher percentages, in all tuberculin dilutions, than the more severe phthisical group, the average size of the reaction, however, being about the same in both groups. Both groups included children and adults, but the proportion of children in the non-pulmonary group was greater. The groups were therefore reshuffled according to age.

Comparison of Tuberculous Adults and Children.

Some of the records did not show clearly whether the patients were children or not, so the groups are smaller through the exclusion of uncertain cases—33 adults and 91 children.

TABLE III.—*Tuberculin Reactions in Tuberculous Adults and Children.*

Tuberculin Dilutions.	Percentages Positive.		Average Size of Reactions in Centimetres.*	
	Adults.	Children.	Adults.	Children.
1 in 10,000	24	40	0.33	0.60
1 in 5,000	54	64	0.80	1.10
1 in 1,000	76	70	1.20	1.50
1 in 500	85	72	1.33	1.80

* Only about 15 patients in each group were "measured" in all dilutions.

The above table suggests that with the higher dilutions tuberculous children react better than tuberculous adults; it will be noticed that the average size of the reaction is slightly greater in children with every strength of tuberculin employed. In this connexion a note by Dr. D. W. Fenwick Jones of the North Wales Sanatorium is of interest. "All babies—surgical—under five," he writes, "reacted well to 1 in 10,000 tuberculin," the reaction appearing late, "only on the sixth day." These infants were further tested with 1 in 5,000, when "they all reacted well on the third day."

This high reactivity of tuberculous infants and children is of importance, especially in view of the fact that non-tuberculous children in the lower age groups differ from healthy adults in giving but a low percentage of "positives." In 28 children "under observation," and without any definite evidence of tuberculous disease, only 7, or 25 per cent., reacted to the intradermal tuberculin test.

Analysis of "Classified" Cases of Pulmonary Tuberculosis.

With the idea, above mentioned, of comparing the tuberculin sensitivity in the more severe and the less severe types, an attempt was made to have the pulmonary cases classified on a system described by me⁵ in 1924; but unfortunately only a very small number of cases were so classified amongst the tested patients. The results are given for what they are worth, but it is recognized that the numbers are too small to be satisfactory. All the classified cases were in the third stadium of phthisis, that is to say, suffering from advanced disease. Twenty were of the "recrudescent" or "C" type, twelve of the "initial" or "A" type. The results of the tuberculin tests are given in the following table.

TABLE IV.—*Tuberculin Reactions in "A" Initial and "C" Recrudescent Cases.*

Type of Case.	Total No. of Cases.	Percentages Positive in each Dilution.			
		1 in 10,000.	1 in 5,000.	1 in 1,000.	1 in 500.
"A"	12	16	33	50	50
"C"	20	15	45	65	90

Admitting that the numbers are too small for a conclusive comparison, the tendency seems to be in the direction of more marked reactions in the more favourable "recrudescent" group. The classified cases were separated into fresh groups for consideration from another point of view, according to the classification of Inman, who divided tuberculous cases, in terms of their degree of auto-inoculation as indicated by their temperatures, into "resting febrile," "ambulant febrile," and "ambulant afebrile." Of the 32 patients, 20 were "resting febrile" and 12 "ambulant afebrile." It should be noted that, though the numbers are the same, the cases divided up quite differently from the divisions in Table IV, nearly all the "A" cases being in the "resting febrile" group.

TABLE V.—*Tuberculin Reactions in "Resting Febrile" and "Ambulant Afebrile" Cases.*

Type of Case.	Total No. of Cases.	Percentages Positive in each Dilution.			
		1 in 10,000.	1 in 5,000.	1 in 1,000.	1 in 500.
Resting febrile ...	20	14	38	62	81
Ambulant afebrile	12	16	58	83	100

Again it must be recalled that the numbers are very small; but the figures suggest that the patients sufficiently resistant to hold their temperature in control are also the patients with a sharp power of reaction to tuberculin.

Summary and Conclusions.

It would seem from the above observations that tuberculin sensitivity is at its height in healthy but infected adults, and is still high in those tuberculous persons in whom the disease is taking a relatively benign course, and that it tends to diminish with the gradual deterioration of health consequent on advancing tuberculosis. Whether this fall in sensitivity is the result of the production of antibodies capable of neutralizing tuberculo-toxin, or whether it is due to a gradual loss of the power of breaking down tuberculin into its toxic derivatives remains uncertain. The fact that long-continued tuberculin therapy may lead to a toleration of tuberculin, with a corresponding clinical improvement, supports the possibility of a "neutralization" factor, at least in favourable cases, while the fall of tuberculin sensitivity in the advanced stages of non-tuberculous diseases, as well as in the terminal stages of tuberculosis, speaks for a gradual deterioration in the power to deal with tuberculin or to react to it. It may be that the loss of tuberculin sensitivity is due not to one but to several factors, and that different factors may be operative in inhibiting the

reaction at different stages of the disease. While it appears certain that a very low percentage of "positive" reactions in any given community goes with a marked racial and individual susceptibility to tuberculosis, it would be a mistake to assume that a high percentage necessarily denotes the possession of a good resistance. The fact that tuberculous children tend to react as well as, or better than, tuberculous adults is against this, since children exhibit a greater liability than adults to generalized tuberculous lesions. It should be recalled, in this connexion, that artificially infected guinea-pigs, though doomed to progressive disease and a fatal termination, almost always show a marked tuberculin sensitivity in the third or fourth week after infection.

A good tuberculin reaction, then, is no guarantee that the patient will be able to control his tuberculosis, nor is a high percentage of reactions, even to so small a quantity of tuberculin as 0.1 c.cm. of a 1 in 10,000 dilution, or 0.01 mg., to be interpreted as meaning that the tested group is necessarily resistant to the evolution of the disease.

With regard to the loss of sensitivity during the progress of a tuberculous infection, the findings of Henry Stuart Willis⁶ suggest that, in guinea-pigs chronically infected by inoculation with an attenuated strain, sensitivity is gradually lost, but may be rapidly "whipped up" again by a reinfection. This type of fall in sensitivity probably depends on a "locking up" of the tuberculous foci in the course of spontaneous cure, and is to be distinguished from the "wearing out" of sensitivity in the terminal stages of tuberculosis; the latter being of serious prognostic import.

It is to be noted that no concentrations stronger than 1 in 500 tuberculin were used. The steady rise in the percentages of "positives" with the stronger concentrations justifies the belief that, as found by Happ and Casparis,³ it should be possible to obtain a positive result in every case, no matter how far advanced, if still stronger tuberculin were given intradermally. In such attempts, however, the possibility of dangerous constitutional reactions should not be lost sight of.

The fact that much larger doses of tuberculin can be tolerated without a general reaction by the intradermal than by the subcutaneous route should recommend the Mendel-Mantoux method to those using tuberculin in treatment.

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PHYSIO-THERAPY IN THE TREATMENT OF
CHRONIC RHEUMATISM.

BY

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THE term "chronic rheumatism," as used somewhat vaguely to cover a number of conditions affecting the joints, muscles, and other skeletal structures, is unfortunate, because it presupposes that these have a pathology identical with that of acute rheumatic fever, a disease which attacks children most frequently, and whose chief ravages fall on the heart. Certain symptoms characteristic of acute rheumatic fever are indeed present in at least one form of chronic rheumatism, but the facts as a whole do not warrant the assumption of a common origin to all forms of rheumatic disease.

The chief lesson to be drawn from modern investigation of rheumatic conditions is the fact that their causes are multiple, just as their manifestations are various, and that each group of cases must be treated according to its individual requirements. The recognition of the important part played by focal sepsis as an etiological factor was a